AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of assessing a disease condition in an individual comprising;

contacting ~~said~~ nucleosomes from a biological fluid sample obtained from the individual with an antibody which binds specifically with a modified histone protein, wherein the modified histone is H4 and is acetylated at a lysine residue corresponding to position 16 of SEQ ID NO:12 or wherein the modified histone is H3 and is methylated at a lysine residue corresponding to position 79 of SEQ ID NO:11,

wherein binding of said antibody to said nucleosomes is indicative that the individual has a disease condition.

2. (Original) A method according to claim 1 wherein said nucleosomes are concentrated from the biological fluid sample.

3. (Previously Presented) A method according to claim 1 wherein the disease condition is a cancer condition or an autoimmune disease.

4.-5. (Cancelled).

6. (Previously Presented) A method according to claim 1 wherein said antibody comprises a detectable label.

7. (Currently Amended) A method of assessing a disease condition in an individual, the method comprising: ~~histone modification in nucleosomes in a biological fluid sample from an individual comprising;~~

contacting a biological fluid sample from said individual with a first antibody,

determining binding of said first antibody to a nucleosome containing a histone modification using a second antibody,

wherein one of said first or second antibodies binds to a nucleosome and the other of said first or second antibodies binds specifically to a modified histone and

wherein the binding of said first antibody and said second antibody to a nucleosome containing a histone modification in said sample is indicative that said individual has a disease condition.

8. (Original) A method according to claim 7 wherein said first antibody binds to nucleosomes and the second antibody binds specifically to the modified histone.

9. (Original) A method according to claim 7 wherein the second antibody binds to nucleosomes and the first antibody binds specifically to the modified histone.

10. (Currently Amended) A method according to claim 7 wherein the modified histone comprises a modification ~~shown in Table 1.~~selected from the group consisting of:

(a) methylation of H3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO:11;

(b) methylation of H3 at a lysine residue corresponding to the lysine residue at position 4, 9, 14, 23, 27, 36, or 79 of SEQ ID NO:11;

(c) acetylation of H3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23, 27, 115 or 122 of SEQ ID NO:11;

(d) phosphorylation of H3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:11;

(e) phosphorylation of H3 at a threonine residue corresponding to the threonine residue at position 3, 11 or 118 of SEQ ID NO:11;

(f) methylation of H4 at an arginine residue corresponding to the arginine residue at position 3 or 92 of SEQ ID NO:12;

(g) methylation of H4 at a lysine residue corresponding to the lysine residue at position 12, 20, 59 or 79 of SEQ ID NO:12;

(h) acetylation of H4 at a lysine residue corresponding to the lysine residue at position 5, 8, 12, 16, 20, 77 or 79 of SEQ ID NO:12;

(i) phosphorylation of H4 at a serine residue corresponding to the serine residue at position 1 or 47 of SEQ ID NO:12;

(j) methylation of H2A at a lysine residue corresponding to the lysine residue at position 99 of SEQ ID NO:13;

(k) acetylation of H2A at a lysine residue corresponding to the lysine residue at position 5, 9, 13, 15, 36 or 119 of SEQ ID NO:13;

(l) phosphorylation of H2A at a serine residue corresponding to the serine residue at position 1 of SEQ ID NO:13;

(m) ubiquitination of H2A at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:14;

(n) methylation of H2B at an arginine residue corresponding to the arginine residue at position 99 of SEQ ID NO:14;

(o) methylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 23 or 43 of SEQ ID NO:14;

(p) acetylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 12, 15, 20, 24, 85, 108, 116 or 120 of SEQ ID NO:14;

(q) phosphorylation of H2B at a serine residue corresponding to the serine residue at position 14, 32 or 36 of SEQ ID NO:14;

(r) ubiquitination of H2B at a lysine residue corresponding to the lysine residue at position 120 of SEQ ID NO:14;

(s) phosphorylation of H2A.X at a serine residue corresponding to the serine residue at position 1 or 139 of SEQ ID NO:15;

(t) phosphorylation of H2A.X at a threonine residue corresponding to the threonine residue at position 136 of SEQ ID NO:15;

(u) ubiquitination of H2A.X at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:15;

(v) acetylation of H2A.X at a lysine residue corresponding to the lysine residue at position 5 or 9 of SEQ ID NO:15;

(w) methylation of H3.3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO: 16;

(x) methylation of H3.3 at a lysine residue corresponding to the lysine residue at position 4, 9, 14, 18, 27, 36, 37 or 79 of SEQ ID NO: 16;

(y) acetylation of H3.3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23 or 27 of SEQ ID NO:16;

(z) phosphorylation of H3.3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:16; and

(aa) phosphorylation of H3.3 at a threonine residue corresponding to the threonine residue at position 11 of SEQ ID NO:16.

11. (Currently Amended) A method according to claim 7 wherein the modified histone comprises a modification selected from the group consisting of:

(a) methylation of H3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO:11;

(b) methylation of H3 at a lysine residue corresponding to the lysine residue at position 14, 23 or 79 of SEQ ID NO:11;

(c) acetylation of H3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23, 27, 115 or 122 of SEQ ID NO:11;

(d) phosphorylation of H3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:11;

(e) phosphorylation of H3 at a threonine residue corresponding to the threonine residue at position 3, 11 or 118 of SEQ ID NO:11;

(f) methylation of H4 at an arginine residue corresponding to the arginine residue at position 92 of SEQ ID NO:12;

(g) methylation of H4 at a lysine residue corresponding to the lysine residue at position 12, 59 or 79 of SEQ ID NO:12;

(h) acetylation of H4 at a lysine residue corresponding to the lysine residue at position 8, 12, 16, 20, 77 or 79 of SEQ ID NO:12;

(i) phosphorylation of H4 at a serine residue corresponding to the serine residue at position 1 or 47 of SEQ ID NO:12;

(j) methylation of H2A at a lysine residue corresponding to the lysine residue at position 99 of SEQ ID NO:13;

(k) acetylation of H2A at a lysine residue corresponding to the lysine residue at position 5, 9, 13, 15, 36 or 119 of SEQ ID NO:13;

(l) phosphorylation of H2A at a serine residue corresponding to the serine residue at position 1 of SEQ ID NO:13;

(m) ubiquitination of H2A at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:14;

(n) methylation of H2B at an arginine residue corresponding to the arginine residue at position 99 of SEQ ID NO:14;

(o) methylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 23 or 43 of SEQ ID NO:14;

(p) acetylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 12, 15, 20, 24, 85, 108, 116 or 120 of SEQ ID NO:14;

(q) phosphorylation of H2B at a serine residue corresponding to the serine residue at position 32 or 36 of SEQ ID NO:14;

(r) ubiquitination of H2B at a lysine residue corresponding to the lysine residue at position 120 of SEQ ID NO:14;

(s) phosphorylation of H2A.X at a serine residue corresponding to the serine residue at position 1 or 139 of SEQ ID NO:15;

(t) phosphorylation of H2A.X at a threonine residue corresponding to the threonine residue at position 136 of SEQ ID NO:15;

(u) ubiquitination of H2A.X at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:15;

(v) acetylation of H2A.X at a lysine residue corresponding to the lysine residue at position 5 or 9 of SEQ ID NO:15;

(w) methylation of H3.3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO: 16;

(x) methylation of H3.3 at a lysine residue corresponding to the lysine residue at position 4, 9, 14, 18, 27, 36, 37 or 79 of SEQ ID NO: 16;

(y) acetylation of H3.3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23 or 27 of SEQ ID NO:16;

(z) phosphorylation of H3.3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:16; and

(aa) phosphorylation of H3.3 at a threonine residue corresponding to the threonine residue at position 11 of SEQ ID NO:16.

~~shown in Table 2.~~

12. (Currently Amended) A method ~~wherein~~ according to claim 7 wherein the biological fluid sample is a plasma or serum sample.

13. (Previously Presented) A method according to claim 7 wherein said first or said second antibody is immobilised.

14. (Original) A method according to claim 13 wherein the non-immobilised antibody of said first and second antibodies comprises a detectable label.

15.-19. (Cancelled).

20. (Currently Amended) A method of diagnosing a cancer condition in an individual comprising;

contacting biological fluid sample obtained from an individual with an antibody which binds specifically to a modified histone, wherein the modified histone is H4 and is acetylated at a lysine residue corresponding to position 16 of SEQ ID NO:12 or wherein the modified histone is H3 and is methylated at a lysine residue corresponding to position 79 of SEQ ID NO:11,

determining the binding of said antibody to nucleosomes in said sample,

the binding of said antibody to nucleosomes in said sample being indicative that said individual has a cancer condition.

21.-24. (Cancelled).

25. (Previously Presented) A method according to claim 20 wherein said antibody comprises a detectable label.

26. (Previously Presented) A method according to claim 1 comprising isolating DNA associated with the nucleosome comprising a modified histone.

27. (Original) A method according to claim 26 comprising amplifying said nucleosome associated DNA.

28. (Previously Presented) A method according to claim 26 comprising sequencing said nucleosome associated DNA.

29. (Previously Presented) A method according to claim 26 comprising labelling said nucleosome associated DNA with a detectable label.

30. (Previously Presented) A method according to claim 26 comprising contacting said nucleosome associated DNA with a DNA molecule having a known sequence under conditions suitable for hybridisation and determining hybridisation.

31. (Original) A method according to claim 30 wherein said DNA molecule of known sequence is comprised in a microarray.

32. (Currently Amended) A method according to claim 26 ~~claim~~ comprising determining the hybridisation of DNA from said individual which is associated with said histone modification relative to DNA associated with said histone modification from one or more other individuals.

33. (Previously Presented) A method according to claim 26 wherein said modified histone comprises a modification associated with gene silencing.

34. (Cancelled).

35. (Previously Presented) A method according to claim 26 wherein said modified histone comprises a modification associated with gene activation.

36. (Cancelled).

37. (Withdrawn) A method of identifying a tumour suppressor gene comprising;

contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with silencing,

isolating nucleosomes bound to said antibody,

sequencing DNA associated with said bound nucleosomes, and;

identifying said DNA as a tumor suppressor gene.

38. (Withdrawn) A method according to claim 37 wherein said modification is selected from H3 Lys 9 (Me) H3 Lys 27(Me), H3 Lys 36(Me), H3 Lys 79(Me) and H4 Lys 20(Me).

39. (Withdrawn) A method of identifying an oncogene comprising;

contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with activation,

isolating nucleosomes bound to said antibody,

sequencing DNA associated with said bound nucleosomes, and;

identifying said DNA as an oncogene.

40. (Withdrawn) A method according to claim 39 wherein said modified histone comprises a modification shown in Table 1 and/or Table 2.

41. (Withdrawn) A method of identifying a patient as a responsive to histone modification modulation therapy comprising;

determining the level of histone modification in cell-free nucleosomes within a sample obtained from the patient, relative to a sample obtained from a healthy individual,

a change in the level of modification being indicative that the patient is responsive to histone modification modulation therapy.

42. (Withdrawn) A method of assessing a patient for a therapeutic treatment comprising;

determining the presence of one or more genes which confer resistance to said treatment in cell-free nucleosomes in a sample obtained from the patient,

wherein said nucleosomes comprise a histone modification associated with activation.

43. (Withdrawn) A method according to claim 42 wherein said modification is a modification shown in Table 1 and/or Table 2.

44. (Original) A method of determining the presence of a cell-free nucleosome having a histone modification comprising;

determining the presence of an antibody which binds specifically to the histone modification in a sample obtained from an individual,

the presence of said antibody being indicative of the presence of said nucleosomes in said individual.

45. (Original) A method according to claim 44 comprising contacting the sample with an antigen comprising a histone modification epitope and determining binding to the antigen.

46. (Original) A method according to claim 45 wherein said antigen is immobilised on a solid support.

47. (Original) A method according to claim 45 wherein said antigen comprises a detectable label.

48. (Currently Amended) A method according to claim 44 wherein said modified histone comprises a modification selected from the group consisting of:

(a) methylation of H3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO:11;

(b) methylation of H3 at a lysine residue corresponding to the lysine residue at position 4, 9, 14, 23, 27, 36, or 79 of SEQ ID NO:11;

(c) acetylation of H3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23, 27, 115 or 122 of SEQ ID NO:11;

(d) phosphorylation of H3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:11;

(e) phosphorylation of H3 at a threonine residue corresponding to the threonine residue at position 3, 11 or 118 of SEQ ID NO:11;

(f) methylation of H4 at an arginine residue corresponding to the arginine residue at position 3 or 92 of SEQ ID NO:12;

(g) methylation of H4 at a lysine residue corresponding to the lysine residue at position 12, 20, 59 or 79 of SEQ ID NO:12;

(h) acetylation of H4 at a lysine residue corresponding to the lysine residue at position 5, 8, 12, 16, 20, 77 or 79 of SEQ ID NO:12;

(i) phosphorylation of H4 at a serine residue corresponding to the serine residue at position 1 or 47 of SEQ ID NO:12;

(j) methylation of H2A at a lysine residue corresponding to the lysine residue at position 99 of SEQ ID NO:13;

(k) acetylation of H2A at a lysine residue corresponding to the lysine residue at position 5, 9, 13, 15, 36 or 119 of SEQ ID NO:13;

(l) phosphorylation of H2A at a serine residue corresponding to the serine residue at position 1 of SEQ ID NO:13;

(m) ubiquitination of H2A at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:14;

(n) methylation of H2B at an arginine residue corresponding to the arginine residue at position 99 of SEQ ID NO:14;

(o) methylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 23 or 43 of SEQ ID NO:14;

(p) acetylation of H2B at a lysine residue corresponding to the lysine residue at position 5, 12, 15, 20, 24, 85, 108, 116 or 120 of SEQ ID NO:14;

(q) phosphorylation of H2B at a serine residue corresponding to the serine residue at position 14, 32 or 36 of SEQ ID NO:14;

(r) ubiquitination of H2B at a lysine residue corresponding to the lysine residue at position 120 of SEQ ID NO:14;

(s) phosphorylation of H2A.X at a serine residue corresponding to the serine residue at position 1 or 139 of SEQ ID NO:15;

(t) phosphorylation of H2A.X at a threonine residue corresponding to the threonine residue at position 136 of SEQ ID NO:15;

(u) ubiquitination of H2A.X at a lysine residue corresponding to the lysine residue at position 119 of SEQ ID NO:15;

(v) acetylation of H2A.X at a lysine residue corresponding to the lysine residue at position 5 or 9 of SEQ ID NO:15;

(w) methylation of H3.3 at an arginine residue corresponding to the arginine residue at position 2, 17 or 26 of SEQ ID NO: 16;

(x) methylation of H3.3 at a lysine residue corresponding to the lysine residue at position 4, 9, 14, 18, 27, 36, 37 or 79 of SEQ ID NO: 16;

(y) acetylation of H3.3 at a lysine residue corresponding to the lysine residue at position 9, 14, 18, 23 or 27 of SEQ ID NO:16;

(z) phosphorylation of H3.3 at a serine residue corresponding to the serine residue at position 10 or 28 of SEQ ID NO:16; and

(aa) phosphorylation of H3.3 at a threonine residue corresponding to the threonine residue at position 11 of SEQ ID NO:16.

~~shown in Table 1 and/or Table 2.~~